

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SAMSUNG BIOEPIS CO., LTD.

Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.

Patent Owner.

Patent No. 11,253,572

Inter Partes Review No. IPR2023-00884

DECLARATION OF GEORGE YANCOPOULOS, M.D., PH.D.

I, George Yancopoulos, M.D., Ph.D., declare as follows:

I. BACKGROUND

1. I have personal knowledge of the facts contained in this Declaration, and if called upon to do so, I could and would testify competently thereto.

2. I am the sole inventor on U.S. Patent No. 11,253,572 (“the ’572 patent”). Ex.1001.

3. I was raised in New York City and attended its public schools, eventually being accepted to The Bronx High School of Science, where I graduated as valedictorian. I received my Bachelor of Arts degree in Biochemistry from Columbia College, where I also graduated as valedictorian. I received my M.D. from Columbia University’s College of Physicians and Surgeons, and I received my Ph.D. in Biochemistry and Molecular Biophysics from Columbia University’s Graduate School of Arts and Sciences. In 1989, I became the Co-Founder and founding scientist of Regeneron Pharmaceuticals, where I currently serve as President, Chief Scientific Officer, and Board Co-Chair of Regeneron.

4. Over the course of my career, I have received numerous honors and awards, including the Prix Galien USA Best Biotechnology Product in 2022, the Prix Galien Roy Vagelos Pro Bono Humanum Award in 2021, Fortune’s World’s 25 Greatest Leaders: Heroes of the Pandemic in 2020, Forbes America’s 100 Most Innovative Leaders in 2019, the Legends in Leadership Award, Yale School of

Management, CEO Institute in 2017, and the Ernst & Young Life Sciences Entrepreneurs of the Year National Award in 2016. During the 1990's, I was among the ten most highly cited scientists in the world.

5. In addition to the '572 patent, I am also named as an inventor of more than 100 patents. I am the principal inventor of the aflibercept composition of matter and several other important medicines, such as the world's leading medicine for allergic diseases (DUPIXENT®) and the first antibody cocktail treatment for COVID (REGN-COV®) for which Regeneron received the U.S. Patent and Trademark Office Patents for Humanity Award in 2020.

6. I have personal knowledge of Exhibits 2005-2007, 2009-2011, 2015, 2017-2020, 2024, 2035, 2039-2045, and 2069-2075 cited in this declaration, which are true and correct copies or excerpts of documents I received, sent, or reviewed. They also are business records created during the ordinary course of Regeneron's business operations and documenting various activities and product development, as is and was our practice at Regeneron.

II. DEVELOPMENT TIMELINE OF EYLEA®

7. Aflibercept is a fusion protein, which I designed and led the clinical development of, that inhibits vascular endothelial growth factor. Aflibercept is the active ingredient in Regeneron's EYLEA® product, which is FDA-approved for the treatment of various angiogenic eye disorders. During clinical trials,

Regeneron used the name "VEGF Trap-Eye" for the drug later known as EYLEA® (aflibercept). I also use that terminology in this Declaration, and any reference to VEGF Trap-Eye below should be understood to refer to aflibercept.

8. Prior to FDA approval of EYLEA®, Regeneron conducted clinical trials to test the safety and efficacy of VEGF Trap-Eye for, among other indications, neovascular age-related macular degeneration (“wet AMD” or “AMD”) and diabetic macular edema (“DME”). As I noted above, I led the scientific and clinical development of VEGF Trap-Eye, including overseeing the clinical trial programs directed to AMD and DME, key portions of which are briefly summarized below.

A. Phase I AMD Clinical Trial – CLEAR-IT-1

9. Regeneron conducted a Phase I clinical trial called CLEAR-IT-1 to test the safety and tolerability of VEGF Trap-Eye in patients with AMD. Ex.1027. In CLEAR-IT-1, a single intravitreal injection of 0.05, 0.15, 0.5, 1, 2, or 4 mg of VEGF Trap-Eye was administered to 21 subjects with AMD. Ex.1027. The CLEAR-IT-1 study detected improvements in both retinal and visual acuity in patients with AMD following a single intravitreal injection of VEGF Trap-Eye. In May 2006, Regeneron issued a press release announcing positive preliminary results at a population level. Ex.1027.

B. Phase I DME Clinical Trial – CLEAR-IT-DME

10. In April 2006, Regeneron began its Phase I clinical trial, CLEAR-IT-DME, to test the safety and tolerability of VEGF Trap-Eye in 5 subjects suffering from DME. Ex.2012, 4. As shown in Exhibit 2012, which is a printout from ClinicalTrials.gov summarizing the CLEAR-IT-DME protocol, each subject in the study received a single 4 mg intravitreal injection of VEGF Trap-Eye. Ex.2012. The single injection resulted in an increase in best corrected visual acuity (BCVA) of 6 to 10 letters for 4 of the subjects. Ex.1030. The study also observed regression in BCVA at 6 weeks. Ex.1009, 3.

C. Phase II AMD Clinical Trial – CLEAR-IT-2

11. On May 1, 2006, Regeneron also announced the start of a Phase II clinical trial. Ex.1027. The Phase II trial was called CLEAR-IT-2 and tested dosing on a fixed interval followed by dosing on an as-needed (“PRN”) basis in 157 subjects. Ex.1009, 4. The fixed dosing period spanned the first 12 weeks—subjects received either monthly doses of 0.5 mg or 2 mg of VEGF Trap-Eye for a total of 4 injections (initial dose and weeks 4, 8, and 12) or quarterly doses of 0.5, 2, or 4 mg of VEGF Trap-Eye for a total of 2 injections (initial dose and week 12). Ex.2004. After the fixed dosing period, the subjects were treated on an as-needed basis with the same dose they received during the fixed dosing period. Ex.1009.

D. Regeneron & Bayer Collaboration

12. In October of 2006, while the CLEAR-IT-2 study was underway, Regeneron entered into a collaboration with Bayer Schering Pharmaceuticals, now called Bayer, for the global development and commercialization of VEGF Trap-Eye. We decided to partner with Bayer because, at that time, Regeneron was still a relatively small company and Bayer had the experience and resources needed to execute and fund the global clinical trials that we wanted to pursue. To the collaboration, Regeneron brought VEGF Trap-Eye, a clinically validated molecule, as well as its extensive knowledge and experience in developing therapies for diseases, including angiogenic eye disorders like AMD and DME.

13. Regeneron's primary reason for collaborating with Bayer was to ensure that we had the resources needed to commercialize a drug and compete against more established companies like Genentech. This was very important because in June 2006, Genentech had received the first approval of a biologic anti-VEGF agent for ophthalmic use, Lucentis®, and we needed a better strategy and more resources to compete with Genentech. We believed that combining Regeneron's scientific expertise regarding VEGF Trap-Eye with Bayer's global infrastructure and experience with commercializing drugs would maximize the likelihood of succeeding commercially. Ex.2068. Under the terms of the collaboration, Bayer agreed to an initial payment to Regeneron of \$75M upfront

and then to share the global development costs in exchange for a share of profits from any drug that ultimately became commercialized. Ex.2068.

14. As part of the collaboration, Regeneron and Bayer established several joint committees to execute the global development of VEGF Trap-Eye. Ex.2069. I served as co-chair of the Joint Steering Committee (JSC), which included an equal number of senior-level members from both companies and was responsible for directing and supervising the collaboration. Ex.2069, 5-7. Various sub-committees—the joint development committee, the joint commercialization committee, and the joint finance committee—were also established and reported to the JSC. Ex.2069, 9. Typically, the sub-committees would prepare information, presentations, and the like to share with the JSC, which made final decisions relating to our development and commercialization efforts. Ex.2069, 4. Exhibit 2069, a November 8, 2006 PowerPoint presentation, further describes the JSC's structure.

15. Consistent with the goal of the collaboration that I explained above, we and Bayer understood that [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]. I was serving as Regeneron's Chief Scientific Officer at the time, a position I continue to hold to this day, [REDACTED]

[REDACTED]

[REDACTED]

III. THE "2Q8" DOSING REGIMEN

16. In my role as Chief Scientific Officer of Regeneron, I conceived of the idea to test a VEGF Trap-Eye dosing regimen of 2 mg every 4 weeks for the first three injections, followed by 2 mg every 8 weeks, for the treatment of angiogenic eye disorders, including AMD and DME.

17. My idea was based on several sources of information, including (1) the need to give patients results at least as good as with Lucentis® and, indeed, to give patients a reason to choose VEGF Trap-Eye over Lucentis®, (2) recent clinical trial results for extended dosing regimens of Lucentis®, (3) recent results from Regeneron's phase II CLEAR-IT 2 trial, and (4) careful weighing of the potential advantages of less-frequent dosing against Regeneron's aversion to the risk of negative clinical trial results.

18. I had the idea to try to determine the dosing interval at which Lucentis® fails. This analysis is shown in Exhibit 2007, the February 16, 2007 presentation that I gave to Bayer at the kick-off meeting between Bayer and Regeneron. Ex.2007, 46-47. At that time, recent data from a clinical trial of

Lucentis® for DME had shown that, when injections were administered monthly, subjects gained visual acuity, but when they were dosed every two months, patients would gain visual acuity in the first month after the injection and then lose it over the second month after the injection. Ex.2007, 46-47. Likewise, a regimen of three monthly doses followed by quarterly injections of Lucentis® failed to improve or even maintain vision in subjects with AMD. Ex.2007, 46. From these data, I determined that Lucentis® likely would fail to maintain gains in visual acuity when dosed at two month or longer intervals. Ex.2007, 46-47.

19. By March 22, 2007, shortly after the kick-off meeting with Bayer, I had received the interim results of the Phase II CLEAR-IT-2 trial for AMD. Ex.2005; Ex.2006. Exhibits 2005 and 2006 are an email by myself and an attachment summarizing those results, respectively. Ex.2005; Ex.2006. According to the interim results, the CLEAR-IT-2 trial included two dosing intervals of VEGF Trap-Eye for the first 12 weeks—monthly doses of 0.5, 2, or 4 mg for a total of 4 treatments and quarterly doses of 0.5 or 2 mg for a total of 2 treatments. Subjects in the quarterly dosing groups showed mean improvements in visual acuity, but the gains were lower in these arms than in the monthly dosing arms. Ex.2004, Ex.2006.

20. After I received the interim results of the CLEAR-IT-2 trial, I had the idea to test 2 mg every 4 weeks for the first three injections, followed by 2 mg every 8 weeks in a Phase III AMD trial.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

23. My practice at that time was to study and understand the various considerations relevant to the clinical design and protocol that we were working towards, and I would have thoroughly discussed any of my ideas with the team before making a final decision on clinical trial design. Thus, over the subsequent weeks, my idea to test the 2 mg of VEGF Trap-Eye every 8 weeks following three initial doses administered every 4 weeks was thoroughly discussed with the internal members of the Regeneron team as well as with our collaborators at Bayer. Ex.2008; Ex.2009; Ex.2075. Exhibits 2008, 2009, and 2075 are emails that I sent or received documenting such discussions.

24. For the 2q8 dosing regimen, I believed that we should use a 2 mg dose of VEGF Trap-Eye. Although we had the ability to dose up to 4 mg of VEGF Trap-Eye in one dose, in my judgment, it was not clear that the higher 4 mg dose could provide a clear benefit over the 2 mg dose. In addition, I knew that Phase III

trials sometimes reveal toxicities that smaller phase II trials do not detect. At the time, we were very worried about an increased risk of intraocular toxicities and inflammation, as well as systemic toxicities. Therefore, the lower, 2 mg dose was the appropriate, more conservative, choice.

25. Ultimately, I concluded that an arm of the AMD Phase III clinical trials (“VIEW trials”), and eventually an arm of the DME Phase II trial (“DA VINCI trial”), should test multiple, “loading” doses administered every 4 weeks, followed by “maintenance” doses, administered every 8 weeks. My rationale for using multiple loading doses was that we had observed that monthly dosing could produce gains in visual acuity, but that those visual acuity gains plateaued around the third monthly injection. I also knew that dosing at intervals longer than one month provided some benefit to visual acuity. My hope was that by pivoting to dosing every 8 weeks after initial dosing every 4 weeks, we could achieve significant benefits to visual acuity while also reducing the number of office visits and intravitreal injections patients were required to receive. But at that time, it was still unclear whether the dosing regimen that I envisioned would work.

26. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

A. VIEW Trials and Results

27. The VIEW trials were Phase III clinical trials designed to test the efficacy of VEGF Trap-Eye in patients with AMD. In addition to conceiving of the 2q8 dosing regimen, I played the leading role in designing the VIEW trials and working with other investigators to carry them out and analyze the data.

28. As discussed above, I made the decision to test three, 2 mg VEGF Trap-Eye loading doses administered every 4 weeks followed by 2 mg maintenance doses of VEGF Trap-Eye administered every 8 weeks (the “2q8” arm) in the VIEW trials. This was a new arm that was not previously tested in either of the CLEAR-IT studies. In addition to this new arm, we included two of the arms tested in CLEAR-IT-2, monthly dosing of 0.5 or 2 mg of VEGF Trap-Eye. Ex.2011. According to the VIEW trials’ design, the results of the VEGF Trap-Eye arms would be compared to 0.5 mg monthly Lucentis® (the “Rq4” arm). Ex.2011. At the time I decided test the 2q8 dosing regimen, I was aware that the VEGF Trap-Eye used in the VIEW trials would be formulated [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] Ex.2076, 76. And, given my earlier insight that Lucentis had failed to

sustain gains in visual acuity when dosed at longer intervals, I also made the decision to measure maintenance of visual acuity and change in best corrected visual acuity from baseline in the VIEW trials and to compare those results with the Lucentis arm of those trials. Ex.2007, 46; Ex.2076, 4. I made the final decision to proceed with the VIEW trials according to this design.

29. At the time I made the decision to test the 2q8 dosing regimen in the VIEW trials and through to their completion, [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

30. The first VIEW trial, VIEW 1, included 1200 patients with AMD in the United States and Canada and began dosing patients in August of 2007. Ex.1015, 3. The second VIEW trial, VIEW 2, which enrolled patients in Europe, Asia, Japan, and Latin America began dosing subjects in May 2008. Ex.1015, 3. People with “[a]ctive ocular inflammation in either eye,” or an “[a]ctive ocular or periocular infection in either eye” were excluded from the study. While Regeneron

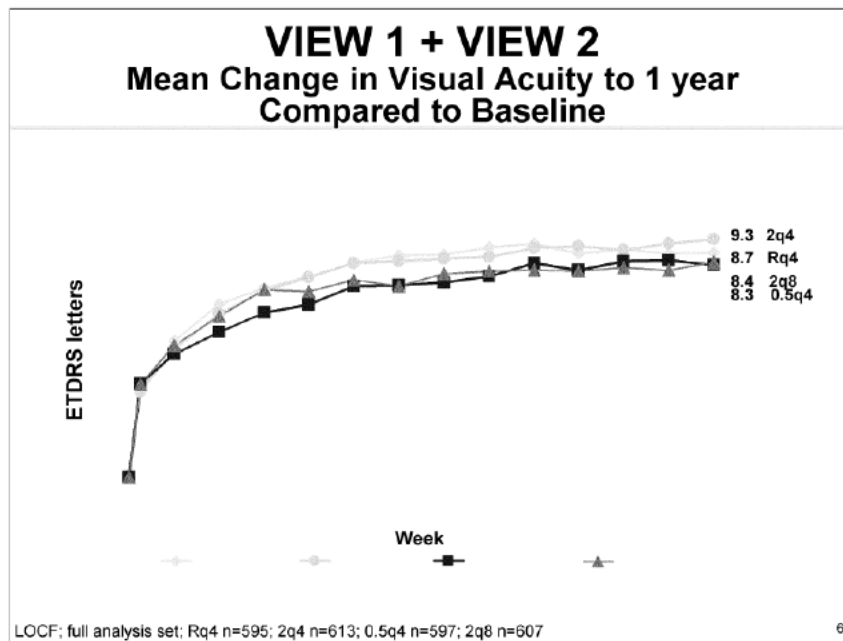
executed the VIEW 1 study in the United States and Canada and Bayer executed the VIEW 2 study abroad, I led the design and analysis plan for both VIEW trials. Ex.1029. I did so with the help of personnel working at my direction to implement all aspects of the trials, from inception through the completion of data analysis.

31. While both VIEW trials were two-year long studies, the primary endpoints of the trials related to the gain and maintenance of visual acuity, including as compared to Lucentis® at 52 weeks. Ex.1029, 1. We completed collection of the 52-week data for both VIEW trials by around October 2010. Ex.2037.

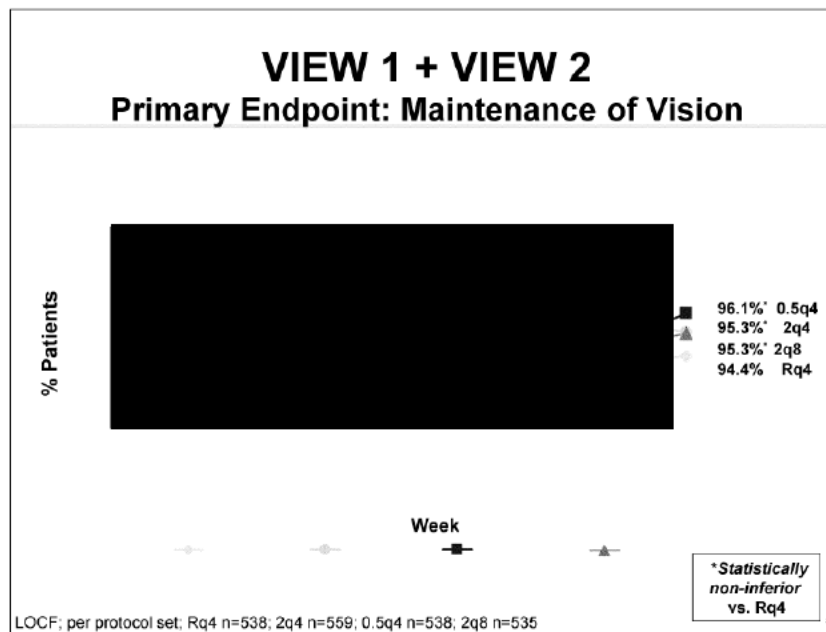
32. Once the results from the VIEW 1 and VIEW 2 trials were available, personnel working at my direction prepared statistical analyses of the results. On November 19, 2010, I received and reviewed Exhibit 2011, a PowerPoint file summarizing the visual acuity results from each VIEW trial, which was attached to Exhibit 2010, an email from one of my colleagues. Ex.2010; Ex.2011. I also received Exhibits 2044 and 2045, an email and an attached draft press release that summarized the same results on that day. Ex.2044, Ex.2045. On November 20, 2010, I requested, received, and reviewed a PowerPoint file (Exhibit 2043) summarizing the combined visual acuity results from both VIEW trials, which was attached to Exhibit 2042, an email from one of my colleagues. Ex.2042; Ex.2043.

33. The goal of the 2q8 VEGF Trap-Eye dosing regimen was to achieve treatment comparable to Lucentis® on a fixed extended dosing interval. That was one way we hoped to differentiate ourselves from Lucentis®. A different goal had been better efficacy than Lucentis®, but we did not see that in the results when we looked at the VIEW 1 and VIEW 2 results combined.

34. By at least November 20, 2010, I had reviewed the VIEW 1 and 2 results, and based on these clinical data, I recognized and appreciated that the 2q8 VEGF Trap-Eye dosing regimen had met that goal of comparable treatment to Lucentis® on a fixed extended dosing interval for subjects with AMD at 52 weeks. Specifically, I recognized and appreciated that the VIEW results indicated that the dosing regimen was both (1) as effective in achieving a gain in visual acuity, and (2) as effective in maintaining visual acuity, as monthly administration of 0.5 mg of Lucentis® by intravitreal injection in human subjects with age-related macular degeneration at 52 weeks following the initial dose:



Ex.2043, 6.



Ex.2043, 5. I also recognized and appreciated that the 2q8 VEGF Trap-Eye dosing regimen achieved a gain in visual acuity of 7.9 and 8.9 letters in VIEW 1 and 2, respectively, that over 90% of patients lost fewer than 15 letters (i.e., “maintenance

of visual acuity”) at 52 weeks, and that these benefits were clinically equivalent and statistically non-inferior to the 8.1 and 9.4 letters visual acuity gains and the over 90% maintenance of visual acuity achieved with 0.5 mg monthly doses Lucentis®:

Confidential					4
VIEW 1 & 2 Results Summary					
	Ranibizumab 0.5 mg monthly	VEGF Trap-Eye 0.5 mg monthly	VEGF Trap-Eye 2 mg monthly	VEGF Trap-Eye 2 mg every 2 months	
Maintenance of vision (% patients losing <15 letters) at week 52 versus baseline					
VIEW 1	94.4%	95.9%*	95.1%*	95.1%*	
VIEW 2	94.4%	96.3%*	95.6%*	95.6%*	
Mean improvement in vision** (letters) at 52 weeks versus baseline (p-value versus ranibizumab 0.5 mg monthly)					
VIEW 1	8.1	6.9 (NS)	10.9 (p<0.01)	7.9 (NS)	
VIEW 2	9.4	9.7 (NS)	7.6 (NS)	8.9 (NS)	
*Visual acuity score was measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) eye chart					
* Statistically non-inferior based on a non-inferiority margin of 10%, using confidence interval approach (95.1% and 95% for VIEW 1 and VIEW 2, respectively)					
*** Test for superiority					
NS=non-significant					

Ex.2011, 4.

35. On November 22, 2010, Regeneron published a press release announcing the positive 1-year results of the VIEW trials. Ex.1007. The information in that press release related to the 2q8 dosing regimen used in the VIEW trials and their results corresponds to the 1-year data of the VIEW trials that I received on November 19, 2010. Ex.2010; Ex.2011. The 2q8 regimen and results reported in the press release are my own work.

B. DA VINCI Trial and Results

36. I also played a critical role in designing the Phase II DA VINCI trial directed to testing VEGF Trap-Eye in subjects with DME and worked with others to carry it out and analyze the data. Like the VIEW trials, the DA VINCI trial was conducted in collaboration with Bayer, with the organizational structure described above.

37. I made the decision to test three 2 mg loading doses administered every 4 weeks followed by 2 mg maintenance doses administered every 8 weeks (the “2q8” arm) in the DA VINCI trial. Ex.2013. Exhibits 2039, 2040, and 2041, an email, memo, and list of action items by myself, respectively, [REDACTED]

[REDACTED]
[REDACTED] Ex.2039; Ex.2040; Ex.2041. Given my earlier insight that Lucentis had failed to sustain gains in visual acuity when dosed at longer intervals, [REDACTED]

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

[REDACTED]. Ex.2048, 88. Regeneron followed the same standard procedure for handling data that I described for the VIEW trials at the time I made the decision to test the 2q8 dosing regimen in the DA VINCI trial and through its completion. I made the final decision to proceed with the DA VINCI trial according to this design.

38. In December 2008, we began enrolling subjects with DME in the Phase II DA VINCI clinical trial. Ex.2014, 2. Enrollment excluded people with “ocular inflammation (including trace or above) in the study eye” and “evidence at examination of infectious blepharitis, keratitis, scleritis, or conjunctivitis in either eye or current treatment for serious systemic infection.” Ex.2048, 37-38.

39. The 221 subjects of the DA VINCI trial were randomly assigned to one of five treatment arms—a laser photocoagulation arm, and four arms directed to VEGF Trap-Eye: (1) 0.5 mg doses every 4 weeks, (2) 2 mg doses every 4 weeks, (3) three 2 mg loading doses administered every 4 weeks followed by 2 mg maintenance doses administered every 8 weeks (the “2q8” arm), and (4) three 2 mg doses every 4 weeks followed by as-needed dosing. Ex.2014.

40. As with the VIEW results, [REDACTED]

[REDACTED]

[REDACTED]

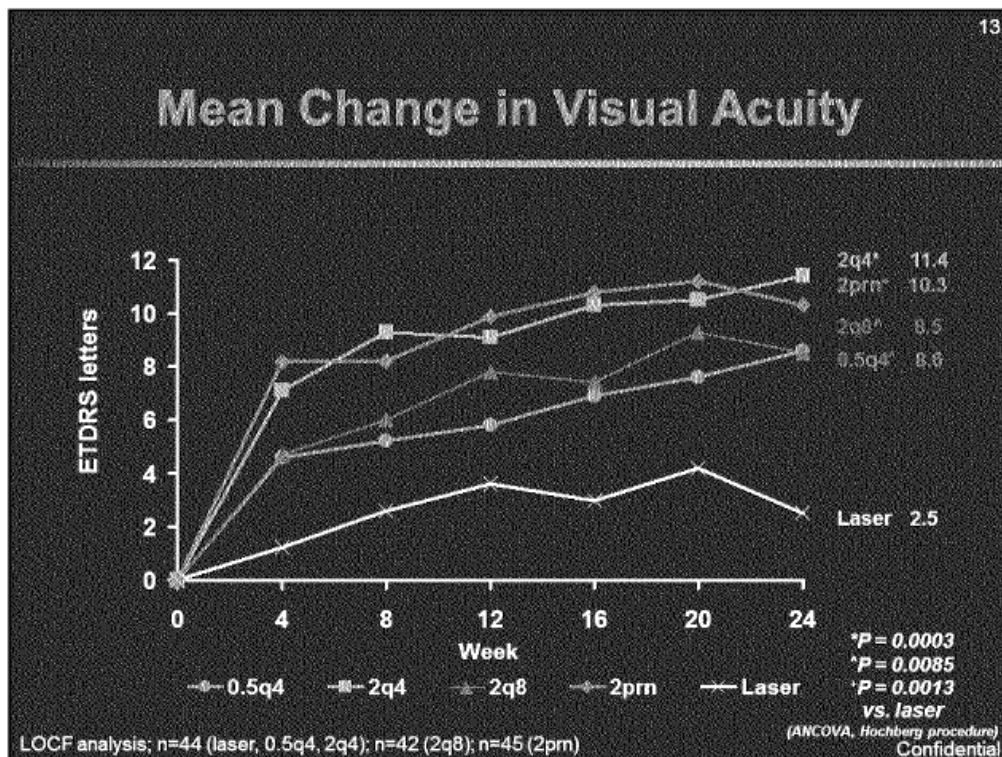
[REDACTED] On February 1 and 2, 2010, I received summaries

of the 24-week data, including statistical analyses [REDACTED]

[REDACTED]

[REDACTED] The following day, I attended a meeting with other members of senior management at Regeneron to review and discuss the 24-week interim results of the DA VINCI trial. Ex.2017. Exhibits 2017, 2018, and 2019 are an email that I received and two attachments summarizing those data, respectively. Exhibit 2035, likewise, is an email from myself attaching the 24-week results.

41. Upon analyzing the 24-week DA VINCI results, and at least by February 2, 2010, I recognized and appreciated that the 2q8 VEGF Trap-Eye dosing regimen would be able to achieve significantly improved visual acuity in patients with DME compared to baseline. Specifically, I recognized that administering the 2q8 VEGF Trap-Eye dosing regimen resulted in an improvement of 9 or more letters in some DME patients as compared to baseline at 24 weeks:



Ex.2019, 13.

42. On February 18, 2010, Regeneron released Exhibit 2020, a press release summarizing the 24-week interim results of the DA VINCI trial, including the visual acuity gains for the various dosing arms. Ex.2020. The 2q8 dosing regimen and visual acuity gains achieved by said dosing regimen that are described in the February 18, 2010 Press Release resulted from my work in designing the clinical trial and analysis plans. The clinical trial and analysis plans were executed by personnel working under my direction. In other words, I was responsible for the scientific aspects of the clinical trial and analysis plan, while administrative aspects of the clinical trials, such as the enrollment of patients and site selection, were carried out by others.

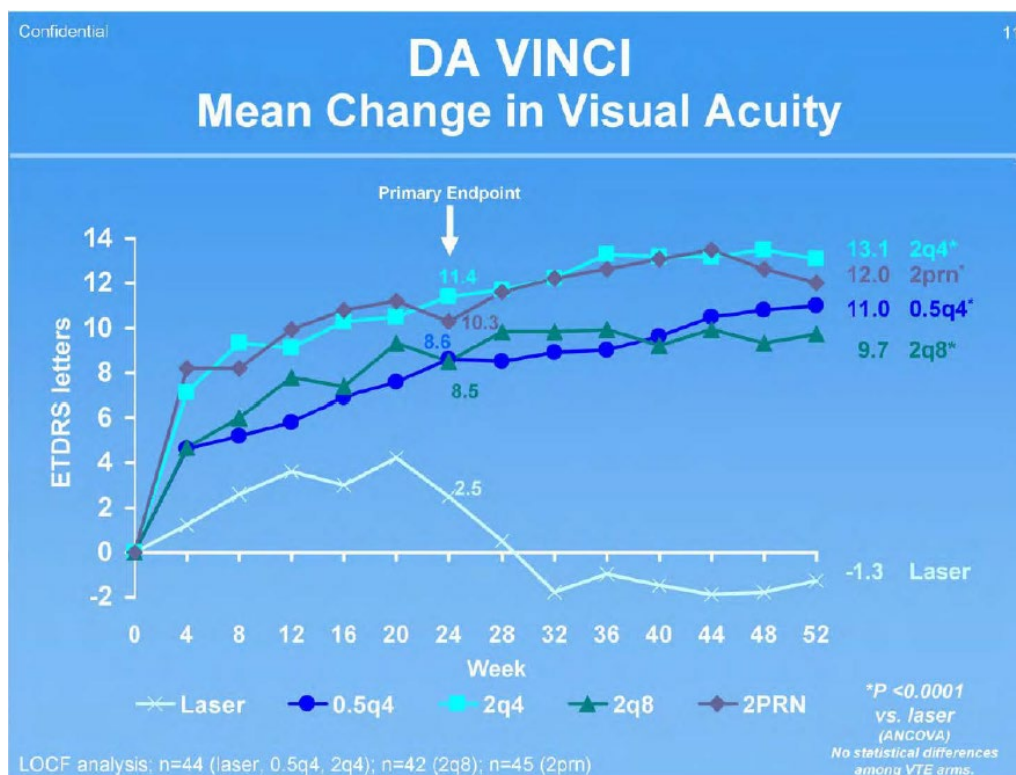
43. I understand that an abstract from the 2010 Association for Research in Vision and Ophthalmology (ARVO) conference has been filed as Exhibit 1010 in this proceeding. I have reviewed that abstract and I understand that it recites some information about visual acuity gains observed at 24-weeks in the DA VINCI trial. The submission of this abstract is consistent with Regeneron's standard practice of arranging for clinical investigators to submit abstracts and present clinical trial results at scientific conferences. It was standard operating procedure for me to review anything that would eventually publish, including abstracts.

44. Like the February 18, 2010 Press Release mentioned above, Exhibit 1010 recites data from the DA VINCI trial related to gains in visual acuity and the change from baseline in central retinal thickness (CRT) at week 24 following treatment. The information in Exhibit 1010 corresponds to the data described in the internal summary of 24-week interim results of the DA VINCI trial emailed to me on February 1, 2010, as described above. Ex.2018, 19, 22-23. Thus, the visual acuity gains (8.5+ letters) observed in subjects receiving the 2q8 dosing regimen in the 2010 ARVO meeting abstract resulted from my work in designing the clinical trial and analysis plans. The clinical trial and analysis plans were executed by personnel working under my direction.

45. On December 1, 2010, the 1-year data for DA VINCI was ready for cleaning, locking, and statistical analysis. Ex.2038, 2. By no later than December

8, 2010, I received Exhibit 2015, a copy of the DA VINCI 1-year results, which was attached to Exhibit 2024, an email from one of my colleagues. Ex.2015; Ex.2024.

46. Upon review of the results, and at least by December 8, 2010, I recognized and appreciated that the 24-week visual acuity gains could be sustained over time using the 2q8 dosing regimen, as evidenced by the mean change in visual acuity at 24-weeks (8.5 letters) versus at 52 weeks (9.7 letters):



Ex.2015, 11.

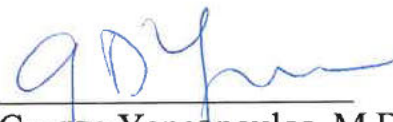
47. On December 20, 2010, Regeneron published the 1-year results of the Phase II DA VINCI trial in a press release. Ex.1006. The information in the December 20, 2010 Press Release corresponds to the data included in the copy of

the DA VINCI 1-year results that I received on December 8, 2010. Ex.2015;
Ex.2024. The DA VINCI 1-year results resulted from my work in designing the
clinical trial, including my idea to test the 2q8 dosing regimen, and related analysis
plans. The clinical trial and analysis plans were executed by people working under
my direction.

IPR2023-00884

I declare that all statements made herein of my own knowledge are true and that all statements made upon information and belief are believed to be true, and that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code.

Dated: 14 Feb 2024


George Yancopoulos, M.D., Ph.D.